DETAILED ACTION

1. Applicant's after final amendment filed 8 May 2008 has been entered. The advisory action dated 3 June 2008 has been withdrawn because the "epoxy-activated support", which was indicated as a new limitation, was subject matter in previously presented claims 52 and 53 and were canceled in the after final amendment. Since claims 52 and 53 were not rejected in the previous office action, an office action is issued on the claims presented in the after final amendment dated 8 May 2008.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1, 2, 4, 6 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sjohölm et al. (US 4,061,466) in view of Spring et al. (US 5,643,721) further in view of Degen et al. (US 5,567,615).

Sjohölm et al. teach an apparatus comprising an insoluble support (cross linked agarose or microparticles) having a ligand of bromosulfophthalein, which is capable of being bindable to albumin, attached thereto (bromosulphophthalein is bromosulfophthalein) without being exposed to albumin (particles are capable of absorbing albumin, but are not present when bromosulphophthalein is attached to the particle, example 9, col. 9, lines 34-43). Sjohölm et al. fail to teach the ligand attached to the support via an epoxy linkage.

Spring et al. teach ligands attached to an agarose substrate by an epoxy linker may be an agarose substrate (col. 5, lines 50-55), in order to provide a mixture that dries in a film form on the surface to which it is applied.

Degen et al. teach a ligand having a hydroxyl group (col. 12, line 46) attached to a polymer support via an epoxy linker (col. 12, lines 41-47) and therefore teach attachment of a ligand that is epoxy-activated (epoxy linker activates the support, col. 13, lines 44-46), in order to provide attachment of ligands to a polymer substrate.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the apparatus of Sjohölm et al., an epoxy linkage between the ligand and the agarose support as taught by Spring et al., in order to provide a simple method of attaching ligands having a hydroxyl group to a substrate by way of a spontaneous covalent attachment as taught by Degen et al. Degen et al. do not specifically teach a bromosulphophthalein ligand being attached to an agarose support. However, Degen et al. teach

that epoxy linker attachment is advantageous for ligands having a hydroxyl group and Spring et al. teach that an epoxy linker is advantageous to link ligands to an agarose support. Since bromosulphophthalein comprises a hydroxyl group, Degen et al. teach the epoxy linkage would be a simpler and advantageous method of attachment of bromosulphophthalein to a substrate, and Spring et al. teach that it would have been obvious for the substrate that the epoxy linker attaches to, to be an agarose support. Therefore an epoxy linker is advantageously used to attach the ligand to the agarose substrate of Sjohölm et al.

With respect to claims 2, 4 and 6, Sjohölm et al. teach the support contained within a container (particles are in a container, col. 4, lines 60-67) and the container being a bottle (beaker is a bottle, col. 8, lines 23-26). Sjohölm et al. also teach the support being a matrix (polyethylene glycol is a matrix and entrapped in the particles, col. 9, lines 39-43).

2. Claims 1-6, 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grahnén et al. (The preparation of Ligandin with Glutathione-S-Transferase Activity from Porcine Liver Cytosol by Affinity Chromatography on Bromosulphophthalein-Sepharose, 1977, Eur. J. Biochem., Issue 80, pages 573-580) in view of Spring et al. (US 5,643,721) further in view of Degen et al. (US 5,567,615).

Grahnén et al. teach an apparatus comprising an insoluble support (sepharose column) having a ligand consisting of bromosulfophthalein attached thereto, which is capable of being bindable to albumin, without being exposed to albumin (pg. 574, section: *Preparation of Bromosulphophthalein Affinity Column*) in view of Degen et al. (US 5,567,615). Grahnén et al. fail to teach the ligand attached to the support via an epoxy linkage.

Spring et al. teach ligands attached to an agarose substrate by an epoxy linker may be an agarose substrate (col. 5, lines 50-55), in order to provide a mixture that dries in a film form on the surface to which it is applied.

Degen et al. teach a ligand having a hydroxyl group (col. 12, line 46) attached to a polymer support via an epoxy linker (col. 12, lines 41-47) and therefore teach attachment of a ligand that is epoxy-activated (epoxy linker activates the support, col. 13, lines 44-46), in order to provide attachment of ligands to a polymer substrate.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the apparatus of Grahnén et al., an epoxy linkage between the ligand and the agarose support as taught by Spring et al., in order to provide a simple method of attaching ligands having a hydroxyl group to a substrate by way of a spontaneous covalent attachment as taught by Degen et al. Degen et al. do not specifically teach a bromosulphophthalein ligand being attached to an agarose support. However, Degen et al. teach that epoxy linker attachment is advantageous for ligands having a hydroxyl group and Spring et al. teach that an epoxy linker is advantageous to link ligands to an agarose support. Since bromosulphophthalein comprises a hydroxyl group, Degen et al. teach the epoxy linkage would be a simpler and advantageous method of attachment of bromosulphophthalein to a substrate, and Spring et al. teach that it would have been obvious for the substrate that the epoxy linker attaches to, to be an agarose support. Therefore an epoxy linker is advantageously used to attach the ligand to the agarose substrate of Grahnén et al.

With respect to claims 2-6 and 25-27, Grahnén et al. teach that the insoluble support is contained in and supported in a column (affinity column with bromosulphophthalein as a ligand,

pg. 574, section: *Preparation of Bromosulphophthalein Affinity Column*; and pg. 575, right column, last 2 paragraphs).

3. Claims 24 and 27-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pieper et al. (US 2002/0127739) in view of Grahnén et al. (The preparation of Ligandin with Glutathione-S-Transferase Activity from Porcine Liver Cytosol by Affinity Chromatography on Bromosulphophthalein-Sepharose, 1977, Eur. J. Biochem., Issue 80, pages 573-580) further in view of Spring et al. (US 5,643,721) and Degen et al. (US 5,567,615).

Pieper et al. teach a column comprising one or more additional supports capable of binding one or more non-albumin proteins (par. 0067), wherein the supports include one or more supports capable of binding IgA and IgG (different matrices carrying different binding agents to remove proteins from a sample is provided at par. 0067; sample proteins of IgG and IgA are non-albumin and are listed at pg. 9, Table 1). Pieper et al. fail to teach a ligand of bromosulfophthalein.

Grahnén et al. in view of Spring et al. further in view of Degen et al., as applied to claim 1, teach a ligand comprising bromosulfophthalein attached to an insoluble support a column (pg. 574, section: *Preparation of Bromosulphophthalein Affinity Column*) via an epoxy linker (Spring and Degen) which produces an epoxy-activated support (Degen), in order to bind albumin.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the column of Pieper et al., a binding agent of bromosulfophthalein as taught by Grahnén et al. in view of Spring et al. further in view of Degen et al., in order to provide a detectable ligand specific to albumin, which strongly influences the

affinity of albumin to the ligand and provides detectable properties upon binding which ensures removal.

Regarding claims 30 and 31, Pieper et al. teach a support bindable to IgA (proteins for which a multi-component antibody affinity matrix are listed at pg. 9, Table 1; IgA has a separate column body par. 0102) and a support bindable to IgG (proteins for which a multi-component antibody affinity matrix are listed at pg. 9, Table 1; IgG has a separate column body par. 0102) wherein the support comprises protein A and G cartridge (a column comprising protein G and A bind IgG; see under Table 1).

Response to Arguments

4. Applicant's arguments filed 8 May 2008 have been fully considered but they are not persuasive. Applicant argues that Sjoholm et al. do not disclose the use of an epoxy-activated insoluble support because the agarose of Sjoholm et al. is crosslinked and therefore the insoluble support is not epoxy-activated. Applicant's argument is not persuasive because Sjohom et al. is not relied upon for teaching the epoxy-activated support.

5. Applicant further argues that Grahnen et al. teach a cross-linked sepharose support, which is not epoxy-activated and Pieper et al. teach a ligand bound to agarose, neither of which are epoxy-activated supports. Applicant's argument is not persuasive because Degen et al. is relied upon for teaching the epoxy-activated support.

6. Furthermore, Degen et al. teach a support with a ligand attached through an epoxy linkage which yields an epoxy activated support. Therefore the epoxy-activated support of the prior art reference of Degen et al. when combined with the supports of Sjoholm et al., Grahnen et

al. and Pieper et al. is the same epoxy-activated support recited in the rejected claims and the rejected claims are not allowable over the prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELANIE YU whose telephone number is (571)272-2933. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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